Deep-brain Stimulation as a treatment for Parkinson's disease

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Introduction:

The Deep-brain stimulation (DBS) is a surgical therapy for the treatment of Parkinson's disease (PD) consisting in the implantation of one or more electrodes in a specific region of the brain. These electrodes attached to leads are connected to an impulse generator, a device that delivers an adjustable electrical current to brain tissue.

The objective of this research project is the explanation of the basis of the treatment along with its benefits and complications.

Pathophysiology of PD:

PD's is a diffuse disease of the central nervous system and the early motor manifestations are usually due to the loss of dopaminergic cells in the substantia nigra pars compacta (SNc). This loss involves an increased activity in certain nuclei causing a decreased motor cortical activity. The basis of this procedure is to disrupt the abnormal neuronal activity to re-establish a more normal motor function.

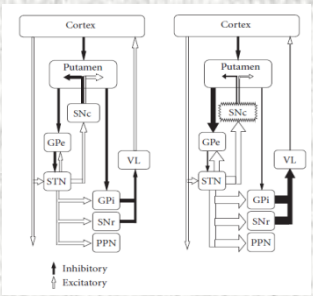

Figure 1: : This model illustrates the different pathways of inhibition and excitation in the basal ganglia differentiating two states. The case shown on the left is from a healthy patient while the one on the right belongs to a patient affected by Parkinson's disease. The figure on the right shows how a change in the content of dopaminergic cells in the SNc originates a smaller inhibitory input to nuclei like Gpi that are also being over stimulated by an increased excitatory input from the STN[1]. (SNc = Substantia nigra pars compacta, GPi = Glubus pallidus pars interna, GPe = Globus pallidus externus , STN = Subtalamic nucleus, SNr = Substantia nigra pars reticulata, PPN = Pedunculopontine nucleus, VL = Ventro lateral nucleus) [1].

Limitations of medical Therapy for PD:

Medical treatment of early PD starts when functional disability appears. Patients have a good initial response to medical therapy which is usually very effective in the early years of PD. This response to medication holds for about 5 years. With progression of the disease, medication related complication develops in a majority of patients until surgical management is suggested.

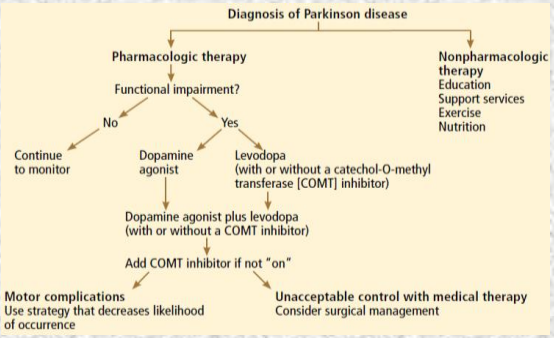

Figure 2: Algorithm for the management of Parkinson's disease. Structured procedure identifying the medical treatment given step by step once the disease is diagnosed. The order of administration of each drug is specific of each stage of the disease until surgical treatment is considered. This surgical treatment is performed once the patient experiences no control even under the effect of medication[2].

Surgical technique:

The DBS devise consists of three components that have to be implanted in a specific location. The electrodes are inserted in the brain and connected to a lead that extends to the outside of the skull and connects with the third component which is the implantable pulse generator usually located in the infraclavicular area.

Figure 3: The lead passes through a hole in the skull and is tunneled under the skin to the scalp, where it is connected to an impulse generator. [3].

Target nuclei:

The most common used targets for patients with PD are the subtalamic nucleus (STN), and the globus pallidus pars interna (GPi), which can be stimulated unilaterally or bilaterally. These intended target locations for the device are used to treat the hallmark symptoms of rigidity, bradikinesia, gait disorder, and tremor.

The ventral intermediate nucleus of the thalamus (VIM) is also being used as a common target to treat essential tremor.

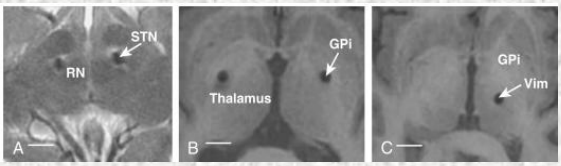

Figure 4: **A to C,** Magnetic resonance images of deep brain stimulation electrodes (*arrows*). There are implanted in three preferred zones: (A) the subthalamic nucleus (STN), (B) globus pallidus (GPi) and (C) ventral intermediate nucleus of the thalamus (Vim). (RN, red nucleus). *Scale bars* = 10 mm[4].

Patients selected for DBS:

A proeoperative evaluation of the patient has to be performed to make sure he/she is a good candidate for this procedure. The parameters taken in account are the following:

Good candidates	• Adequate response to dopaminergic therapy • Presence of on-off fluctuations • Dyskinesia imparing quality of life • Mediaction-resistant tremor • Reasonable cognitive function
Borderline candidates	• Severe dyskinesia with poor on-off dopaminergic response • On-off fluctuations with moderate cognitive function • On-off fluctuations with a poor on-off dopaminergic response • Medication-resistant tremor with moderate cognitive dysfunction • Medication-resistant tremor with poor on-off dopaminergic response
Poor candidates	• Severe dementia • Severe autonomic dysfunction • Poor dopaminergyc response • Atypical parkinsonism • Unstable psychiatric disease • Absence of a dedicated caregiver

Figure 5: Structures table contemplating the characteristics of the candidates for DBS[1].

Complications:

DBS is not an entirely safe procedure yet, it involves many risks and complications that can be divided in 3 stages of the treatment:

Surgical complications:

This stage includes all types of complications that may occur during the surgical intervention. This surgery can cause intracranial and intracerebral hemorrhage, infections, misplacement of the DBS leads, or suboptimal placement of the leads.

Hardware complications:

This type of complications take place after the surgery and include the migration of the leads, DBS lead failure or any other component of the system, skin erosion and pain over the hardware or infection.

Simulation-related complications:

These types of complications are related to problems during the stimulation in the process of the DBS programming. These kinds of complications are reversible with a simple adjustment of the stimulating amplitude.

Conclusions:

-DBS is restricted to patients that have developed motor fluctuations or dyskinesias but still have good cognitive capability.

-The treatment helps patients achieve a reduction of the dose of medication as well as motor fluctuations and an improvement of the symptoms .

-Improvement and complications depend on different factors: stage of the disease, targets of the neurostimulation and electrode position.

- DBS Includes not just the implantation of the hardware but also a postoperative programming and maintenance.

-The actual effect of DBS is still unknown and has to be studied.

References:

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